REMARKS

1. **Priority Claim Under 35 US.C. Section 119**

Page 1 of the Office Action indicates that the Examiner has not received any of the certified copies of the priority documents. The Examiner, however, will note that this application is the national phase of a PCT international application. The priority documents were appropriately submitted to the International Bureau during the international phase, as confirmed by the attached copy of Form PCT/IB/304. As such, it is submitted that Applicants have properly perfected their claim to priority, and the Examiner is requested to correct the record in this regard.

2. **Double Patenting Rejection**

The claims have been rejected for obviousness-type double patenting over claims 1-19 of U.S. Patent No. 6,645,500. This rejection will be addressed and upon the indication of allowable subject matter in the present application.

3. **Rejection Under 35 U.S.C. 112, First Paragraph - Enablement**

Claims 1, 3, 5, 8-12, 17-24, 28 and 57-60 have been rejected under 35 U.S.C. 112, first paragraph. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Claim 1 has been amended to recite that the claimed methods target *mammalian* OPGL, and the amended claim further recites the presence of at least one foreign T helper

epitopes. These amendments appear to address and render moot the Examiner's primary objection to the claims. It should be remembered that the claims relate to a method of immunization, and not to a method of producing the immunogen used in the method. Phrased otherwise, the claimed method relies on the inventive finding that immunogens capable of inducing antibodies cross-reactive with self-OPGL can be used in a method for down-regulation of OPGL whereby diseases such as osteoporosis can be treated - hence, the immunogen used in the claimed method should merely be one that can induce such cross-reactive antibodies.

If one closely studies the formula in claim 1, it is *required* that at least one B-cell epitope in a mammalian OPGL is present and that at least one foreign T-helper epitope is present (either as a side group in one of the $OPGL_{ex}$ fragments or as one of the MOD, fragments). So even assuming arguendo that the Examiner is correct in asserting that protein functionality could be destroyed by introduction of amino acid modifications, the claim *requires* the presence of the minimal number of components necessary to induce a cross-reactive immune response: A B-cell epitope from OPGL and a foreign T helper epitope. That is, while the Examiner asserts concerns about whatever insertions, deletions or other modifications may effect the immunological responses, the claims still require the presence of at least one B-cell epitope and at least one foreign T-helper epitope.

In this context it should be noted that, as opposed to the Examiner's remark in paragraph 15, conjugation is not required to promote immune responses against small peptides, since size of the immunogen is not the main issue. It is sufficient to include a foreign T-helper epitope. This was elucidated in the 1990'ies, when it was discovered that conjugation to larger

protein merely provides for the necessary T-helper epitopes, but one single epitope may be as well-suited as a complete protein, cf. also the description in the present patent where a lengthy discussion of population coverage is provided.

Further, identification of B-cell epitopes in a known protein antigen is not problematic and can be achieved either *in silico* or *in vitro* by simple epitope mapping. Both alternatives are described in the application and would never amount to undue experimentation for the skilled artisan.

In paragraphs 16-18, the Examiner has questioned the effect of the method and the alleged lack of sufficient description with respect to the structure and position of epitope placement an OPGL. But as explained above, the claims define that the modified OPGL (a) contains at least one B-cell epitope and (b) contains at least one foreign T-helper epitope and that the modifications are "introduced between the preserved B-cell epitopes".

With respect to the Examiner's remarks in paragraph 22, it is not correct that the statements in the specification on page 54, lines 10-17 could indicate to the skilled person that an OPGL immunogen targeting e.g. longer or shorter fragments of OPGL should be ineffective or non-enabled. The cited statement merely provides for an identification of a particular embodiment of the invention, but this should hardly be a reason to deny protection for other embodiments. For instance, if one targets other parts of the molecule, this would perhaps not block activity, but antibodies binding an antigen also effect clearance of the antigen whereby a reduction in activity is observed.

With respect to the Examiner's remarks in paragraph 24, while the Hertz declaration refers to a particular disclosed embodiment, in order to reject the claims the Examiner should

provide substantiated reasoning for asserting that the claimed invention is not fully enabled. This the Examiner has not done.

For the above reasons, reconsideration and withdrawal of the enablement rejection are requested.

4. Rejection Under 35 U.S.C. 112, First Paragraph – Written Description

Claims 1, 3, 5, 8-12, 17-24, 28 and 57-60 have been rejected under 35 U.S.C. 112, first paragraph. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner urges that the written description requirement has not been fulfilled because the specification allegedly does not provide "sufficient distinguishing identifying characteristics of the [claimed] genus". The Examiner, however, fails to adequately consider the features which are specifically recited in the claims and are fully supported by the specification. Amended claim 1 does define the claimed genus in terms of:

a. The "starting" OPGL "has amino acid sequences set forth in SEQ ID No. 2 for human OPGL".

b. The modified OPGL polypeptide has modifications, but those are introduced "between the preserved B-cell epitopes".

c. The modified OPGL polypeptide has at least one modification "in the form of at least one foreign T helper lymphocyte epitope".

d. The modified OPGL polypeptide functions by inducing antibodies which bind to the animal's own OPGL, thereby down-regulating OPGL.

Thus, contrary to the Examiner's comments, the claims do indeed recite a combination of structural and functional characteristics that sufficiently define Applicants' generic invention. Accordingly, reconsideration and withdrawal of the rejection are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), Applicants petitioned for an extension of three months to July 31, 2005 for the period in which to file a response to the Office Action dated January 31, 2005 in the concurrently filed Notice of Appeal. The required fee has been paid in connection with the proper filing of this Notice of Appeal.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Certificate of Transmission
I hereby Certify that this correspondence is being facsimile transmitted to the Patent and Trademark Office:
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Respectfully submitted,

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4614-0105P

Attachment(s)

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

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Date of mailing (day/month/year) 13 October 1999 (13.10.99)	
Applicant's or agent's file reference 22021 PC 1	**IMPORTANT NOTIFICATION**
International application No. PCT/DK99/00481	International filing date (day/month/year) 13 September 1999 (13.09.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 15 September 1998 (15.09.98)
Applicant M&E BIOTECH A/S et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
15 Sept 1998 (15.09.98)	PA 1998 01164	DK	30 Sept 1999 (30.09.99)
02 Octo 1998 (02.10.98)	60/102,896	US	01 Octo 1999 (01.10.99)

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Form PCT/IB/304 (July 1998)